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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/725,019	11/29/2000	John E. Thompson	10799/12	8962
26646	7590	10/08/2003	EXAMINER	
KENYON & KENYON ONE BROADWAY NEW YORK, NY 10004			BAUM, STUART F	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 10/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

## Application No.

09/725,019

## Applicant(s)

THOMPSON ET AL.

## Examiner

Stuart F. Baum

## Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 15 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 13,14,16,17,24-27,37-39,48,49,52,53 and 74 is/are pending in the application.

4a) Of the above claim(s) 74 is/are withdrawn from consideration.

- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

- 6) ☒ Claim(s) 13,14,16,17,24-27,37-39,48,49,52 and 53 is/are rejected.

- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***RCE Acknowledgment***

1. The request filed on July 15, 2003 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 09/725019 is acceptable and a RCE has been established. An action on the RCE follows.

2. Claims 13-14, 16-17, 24-27, 37-39, 48-49, 52-53, and 74 are pending.  
Claims 1-12, 15, 18-23, 28-36, 40-47, 50-51, and 54-73 have been canceled.

3. In view of newly added claim 74, the following restriction applies.

I. Claims 13-14, 16-17, 24-27, 37-39, 48-49, 52-53, drawn to an antisense polynucleotide which hybridizes under high stringency conditions with SEQ ID NO:11 a vector comprising said antisense polynucleotide and regulatory sequences, a bacterial cell or plant transformed with said polynucleotide, or a plasmid comprising said polynucleotide and comprising a replication system functional in a prokaryotic host, classified in class 536, subclass 24.5 for example.

II. Claim 74, drawn to an apoptosis-induced cDNA having the sequence of SEQ ID NO:11, classified in class 536, subclass 23.6 for example.

4. Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are distinct one from the other because the starting material, method steps and end

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products are distinct. The antisense sequences of Group I are used for inhibiting the expression or decreasing the expression of a protein whereas the sense sequence of Group II is used for increasing the expression of a protein.

5. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the literature and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

6. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

8. Group I, claims 13-14, 16-17, 24-27, 37-39, 48-49, 52-53 are elected by original presentation. Accordingly, claim 74 is non-elected and will not be examined in the instant application.

9. Claims 13-14, 16-17, 24-27, 37-39, 48-49, and 52-53, are examined in the present office action.

***Specification/Priority***

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 371 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

It is noted that Applicant made a *bona fide* attempt to state the priority in the first line of the specification, but Applicant's priority recitation is missing the date of the second application and Applicant has not stated that serial number 09/597,771 is a CIP of serial number 09/348,675.

***Drawings***

Figures 5, 7, 10, 11-12, and 16-20 are objected to for being too dark. Please submit, high contrast originals.

***Indefiniteness***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 14, 16, 17, 48, and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 14, the metes and bounds of "senescence-induced elf-5a" have not been defined. "senescence-induced elf-5a" is an arbitrary term that Applicants have defined by conditions of isolation. No sequence is set forth and no hybridization conditions are set forth for RNA

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hybridization. Applicants have not explicitly described “senescence-induced elf-5a” in terms of nucleic acid or amino acid sequence or specific function. It is unclear how “senescence-induced eIF-5a” correlates to SEQ ID NO:11. No function is set forth for any antisense sequences. With what gene would the antisense sequence react, or what is the function of the claimed antisense molecule. All subsequent recitations of “senescence-induced elf-5a” are also rejected.

In claims 16 and 17, the recitations “a 5’ non-coding” and “a 3’ end”, respectively, implies there are more than one of each of these regions, which does not appear to be Applicants’ invention.

In claims 48 and 49, it is not clear if the plasmid comprises a replication system comprising an antisense polynucleotide or if the plasmid comprises both a replication system and an antisense polynucleotide. Inserting --(1)-- before “a replication” and inserting --(2)-- before “an antisense” will clarify that the claimed plasmid contains both.

### ***Written Description***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 13-14, 16-17, 24-27, 37-39, 48-49, and 52-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to an antisense polynucleotide which hybridizes with RNA encoding senescence-induced eIF-5A, wherein said antisense polynucleotide hybridizes under high stringency conditions with SEQ ID NO:11 wherein high stringency conditions comprises a 6X SSC hybridization solution, and wherein hybridization is carried out at about 68<sup>0</sup>C, a vector comprising said antisense polynucleotide and regulatory sequences, or wherein the antisense polynucleotide hybridizes to a 5'-non-coding region or 3-end of the RNA encoding senescence-induced eIF-5a, a bacterial cell or plant transformed with said polynucleotide, or a plasmid comprising said polynucleotide and comprising a replication system functional in a prokaryotic host.

Applicants isolated a full-length cDNA clone of SEQ ID NO:11, of a senescence-induced eIF-5A encoding polynucleotide from a cDNA library constructed from tomato leaves.

Applicants claim sequences that hybridize under said stringency conditions with SEQ ID NO:11 but said sequences encompass naturally occurring allelic variants, mutants of eIF-5A, as well as sequences encoding proteins having no known eIF-5A activity, of which Applicant is not in possession. Absent of such disclosure, one skilled in the art cannot determine the genus of sequences based upon the disclosure of the cDNA sequence of SEQ ID NO:11 with any certainty or predictability. Accordingly, the specification fails to provide an adequate written description to support the hybridization language as set forth in the claims.

In addition, Applicant claims an antisense polynucleotide which hybridizes with any RNA encoding any senescence-induced eIF-5A sequence of undisclosed SEQ ID NO, under

unspecified hybridization conditions. Absent any information about the identity of the RNA sequence or the hybridization conditions, one skilled in the art cannot determine or predict the genus of sequences to which Applicants' antisense polynucleotide will bind. Accordingly, the specification fails to provide an adequate written description to support the genus of RNA sequences as specified in the claim. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

#### ***Enablement***

12. Claims 13-14, 16-17, 24-27, 37-39, 48-49, and 52-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained and reiterated because Applicant did not traverse the enablement rejection in the previous office action and Applicants' amendment to claim 14 does not obviate the rejection. The amendment to claim 14 encompasses sequences for which Applicant is not enabled.

The claims are drawn to an antisense polynucleotide which hybridizes under high stringency conditions with SEQ ID NO:11 wherein high stringency conditions comprises a 6X SSC hybridization solution, and wherein hybridization is carried out at about 68<sup>0</sup>C, a vector comprising said antisense polynucleotide and regulatory sequences, or wherein the antisense polynucleotide hybridizes to a 5'-non-coding region or 3-end of the RNA encoding senescence-induced eIF-5a, a bacterial cell or plant transformed with said polynucleotide, or a plasmid



comprising said polynucleotide and comprising a replication system functional in a prokaryotic host.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicants isolated a full-length cDNA clone of the senescence-induced eIF-5A encoding polynucleotide from a cDNA library constructed from tomato leaves, as set forth in SEQ ID NO:11. Applicants do not provide guidance or examples using any antisense construct complementary to their cDNA clone for inhibiting expression of the eIF-5A protein which Applicants purport will ultimately inhibit senescence. Applicants' claims are drawn to a DNA antisense molecule that hybridizes under unspecified conditions with any RNA molecule encoding a senescence-induced eIF-5A. The recitation "antisense" has a functional connotation. Antisense sequences target a particular gene and down-regulate or suppress its activity. The claims set forth that the antisense hybridizes to RNA, but it is unclear what gene is down regulated or suppressed since Applicant has not explicitly defined "senescence-induced eIF-5A". Additionally, since no hybridization conditions are recited, it is unclear what gene(s) the antisense sequence would target. Virtually any sequence would hybridize to the RNA encoding

senescence-induced eIF-5A given the lack of hybridization conditions. Even given the hybridization conditions for the hybridization of the antisense molecule with SEQ ID NO:11, any number of genes would be targets of the antisense sequence, given the lack of hybridization conditions for the RNA molecule. Applicants have not enabled the antisense polynucleotide for all undisclosed sequences.

Applicants claim an antisense polynucleotide that hybridizes to SEQ ID NO:11 under conditions as specified in claim 14. The state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65°C (page 859, left column, 2<sup>nd</sup> paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe. The selected sequences will encode proteins having modifications including additions, deletions, and substitutions of many amino acids when compared to a protein encoded by SEQ ID NO:11. Therefore, it is unpredictable as to whether

any of the antisense molecules will hybridize in vivo to any mRNAs encoding an eIF-5A protein and thus inhibit its expression.

Applicants' claims are drawn to fragments and sequences not exhibiting 100% sequence identity with SEQ ID NO:11. The state-of-the-art teaches using sequences exhibiting below a 100% sequence identity as compared to a reference sequence produces unpredictable RNA degradation results. Moonan et al (2002, Journal of Virology 76(3):1339-1348) teach "sugarcane plants expressing untranslated viral capsid sequences of *Sorghum mosaic virus* strain SCH, challenged with SrMV viruses of strains SCM and SCI and *Sugarcane mosaic virus* strain, show various levels of virus resistance that correlated with the percentage of sequence identity of the transgenes to the sequence of the challenging virus" (page 1347, 1<sup>st</sup> paragraph, right column). Therefore, the protection achieved using sequences that exhibited less than 100% sequence identity to the respective viral gene resulted in an inferior viral protection.

Applicants purport that inhibiting the synthesis of the eIF-5A protein will inhibit senescence. But, Applicants have not reduced to practice their invention. Senescence is a complex, highly regulated process involving multiple proteins in multiple pathways. How senescence occurs is not fully understood to date. It is highly unlikely that one protein controls the senescence process. More likely, there are multiple proteins with redundant functions that are involved in the process to ensure senescence occurs at the appropriate time and place. In addition, if senescence was controlled by a single protein, then mutagenesis experiments should have already uncovered the gene responsible for encoding this protein. But to date, no such gene has been uncovered by chemical or insertional mutageneses. Applicant has not shown that eIF-5A alone can regulate or control senescence by itself. It is unpredictable what other proteins are

required. Given the lack of guidance and the unpredictability of what other proteins are required, excessive experimentation would be required to make and use the claimed invention.

Therefore, given the breath of the claims; the lack of guidance and examples; the unpredictability; and the state of the art as discussed above, undue experimentation would be required by one skilled in the art to obtain an antisense molecule whose corresponding encoding DNA molecule would hybridize to SEQ ID NO:11 and when expressed in plants would inhibit just senescence and not disrupt the normal processes required for plant growth.

***Claim Rejections - 35 USC § 102***

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 13-14, 16-17, 24-27, 37-39, 48-49, and 52-53 are rejected under 35 U.S.C. 102(b) as being anticipated by Grierson et al (June, 1996, U.S. Patent Number 5,530,190).

The claims are drawn to a DNA antisense molecule that hybridizes under unspecified conditions with any RNA molecule encoding a senescence-induced eIF-5A wherein said antisense polynucleotide hybridizes under high stringency conditions with SEQ ID NO:11 wherein high stringency conditions comprises a 6X SSC hybridization solution, and wherein hybridization is carried out at about 68<sup>0</sup>C, wherein the polynucleotide hybridizes to any 5'-non-coding region or any 3'-end of any RNA molecule encoding a senescence-induced eIF-5A, a vector comprising said antisense polynucleotide and regulatory sequences, a bacterial or plant cell transformed with said vector, wherein said plant cell is a flowering plant cell.

Grierson et al teach an antisense ACC oxidase sequence subcloned into a vector that is used to transform tomato to inhibit fruit ripening which is a form of senescence (Columns 6-10).

For purposes of molecular biology, the vector would also be transformed into bacteria. The Office interprets claim 14 to read on any antisense polynucleotide because Applicant does not specify hybridization conditions associated with the hybridization of the antisense polynucleotide with the RNA sequence. In addition, because the recitation "senescence induced eIF-5A" has not been defined as discussed in the 112 2<sup>nd</sup> rejection above, the specified RNA sequence encompasses any RNA sequence, and as such, Grierson et al anticipate the claimed invention.

14. No claims are allowed.


15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 703-305-6997. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stuart F. Baum Ph.D.

October 2, 2003

  
10/6/03  
PHUONG T. BUI  
PRIMARY EXAMINER